BGB-A317-212: A multicenter, open-label, phase II study to evaluate the efficacy and safety of tislelizumab in combination with lenvatinib in patients with selected solid tumors

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Background: Tislelizumab, an anti-programmed cell death protein 1 (PD-1) monoclonal antibody, has demonstrated promising efficacy in several advanced solid tumors. However, some patients (pts) do not respond or develop resistance to tislelizumab monotherapy. Lenvatinib, a receptor tyrosine kinase inhibitor targeting VEGFR 1-3, FGFR 1-4, PDGFR alpha, KIT, and RET, has shown a potential synergistic effect with anti-PD-1 therapy. Here, we report the primary results of a phase II study evaluating the combination of tislelizumab plus lenvatinib in pts with solid tumors (NCT05014828).

Methods: Pts with histologically/cytologically confirmed selected solid tumors, naïve to lenvatinib and anti-programmed death-ligand 1 (PD-L1)/PD-1 therapies were enrolled. Part 1 (safety run-in) determined the recommended phase II dose (RP2D) of lenvatinib in combination with tislelizumab 400 mg IV every 6 weeks. In Part 2 (expansion), pts received lenvatinib at the RP2D from Part 1 (20 mg orally/day) plus tislelizumab per the Part 1 regimen until disease progression, withdrawal, or death. The primary endpoints were safety and RP2D determination (Part 1) and overall response rate (ORR; Part 2).

Results: At data cutoff (Oct 20, 2023; median follow-up 12.1 months [mo; renal cell carcinoma, RCC]; 10.8 mo [head and neck squamous cell carcinoma, HNSCC]; 14.8 mo [gastric cancer, GC], and 22.0 mo [non-small cell lung cancer, NSCLC]), 58 pts were treated in Part 2 (RCC, n=23; HNSCC, n=27; GC, n=3; NSCLC, n=5), 6 of whom were also included in Part 1. The ORR was 66.7% in pts with RCC, 33.3% (HNSCC), 33.3% (GC), and 20.0% (NSCLC). Median duration of response (mDoR) was 18.5 mo and 9.6 mo in pts with NSCLC and HNSCC, respectively; not estimable (NE) for RCC and GC (**Table**). No new safety signals were identified; grade ≥3 treatment-related adverse events were reported in 78.3%, 59.3%, 33.3% and 60.0%, of pts with RCC, HNSCC, GC, and NSCLC, respectively (**Table**).

Conclusions: Tislelizumab plus lenvatinib had a manageable safety profile and showed preliminary antitumor activity in pts with selected tumor types. Longer follow-up is needed to further investigate the potential of this combination to benefit pts with advanced solid tumors.

	RCC	HNSCC	GC	NSCLC
Efficacy-evaluable	**n=21**	**n=24**	**n=3**	**n=5**
ORR, % (95% CI)[a]	66.7 (43.0, 85.4)	33.3 (15.6, 55.3)	33.3 (0.8, 90.6)	20.0 (0.5, 71.6)
mDoR, mo (95% CI)	NE (10.8, NE)	9.6 (2.8, NE)	NE (NE, NE)	18.5 (NE, NE)
Safety-evaluable	**n=23**	**n=27**	**n=3**	**n=5**
Any TRAE, n (%)	22 (95.7)	25 (92.6)	3 (100.0)	5 (100.0)
Grade ≥3	18 (78.3)	16 (59.3)	1 (33.3)	3 (60.0)
Serious	10 (43.5)	10 (37.0)	2 (66.7)	2 (40.0)
Leading to death	1 (4.3)[b]	3 (11.1)[c]	0 (0.0)	0 (0.0)
Leading to treatment discontinuation	3 (13.0)	6 (22.2)	1 (33.3)	1 (20.0)

[a]Confirmed ORR by investigator; [b]Due to organ failure; [c]Due to pneumonia, left carotid hemorrhage and unknown cause

CI, confidence interval.